10/ 507,399

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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 12	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 13	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 14	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 15	AUG 27	USPATOLD now available on STN
NEWS 16	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 17	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 18	SEP 13	FORIS renamed to SOFIS
NEWS 19	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 20	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 21	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 22	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 23	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 24	OCT 19	BEILSTEIN updated with new compounds

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 17:25:03 ON 22 OCT 2007

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 21 OCT 2007 HIGHEST RN 951124-19-9
DICTIONARY FILE UPDATES: 21 OCT 2007 HIGHEST RN 951124-19-9

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http://www.cas.org/support/stngen/stndoc/properties.html

```
=> s glitazone and potassium
             2 GLITAZONE
        124476 POTASSIUM
L1           0 GLITAZONE AND POTASSIUM

=> s glitazone
L2           2 GLITAZONE

=> d scan l2

L2   2 ANSWERS  REGISTRY  COPYRIGHT 2007 ACS on STN
IN   Fluoroglitazone (9CI)
MF   Unspecified
CI   MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2   2 ANSWERS   REGISTRY  COPYRIGHT 2007 ACS on STN
IN   2,4-Thiazolidinedione
MF   C3 H3 N O2 S
CI   COM
```

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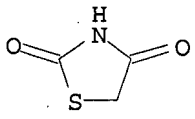

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.75	15.96

FILE 'CAPLUS' ENTERED AT 17:26:28 ON 22 OCT 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 22 Oct 2007 VOL 147 ISS 18
FILE LAST UPDATED: 21 Oct 2007 (20071021/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> a l2
A IS NOT A RECOGNIZED COMMAND
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"HELP COMMANDS" at an arrow prompt (=>).

=> s l2
L3 2013 L2

=> s l3 and polymorph?
218052 POLYMORPH?
L4 34 L3 AND POLYMORPH?

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 34 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1088938 CAPLUS
TITLE: Methods and compositions for controlling body weight and appetite

10/ 507,399

INVENTOR(S): Lippa, Arnold S.; Epstein, Joseph W.; Basile, Anthony; Tizzano, Joseph T.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27pp., Cont.-in-part of U.S. Ser. No. 442,743.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

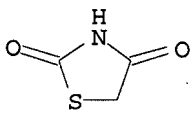
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007225351	A1	20070927	US 2006-603974	20061121
WO 2002066427	A2	20020829	WO 2002-US845	20020111
WO 2002066427	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004132797	A1	20040708	US 2004-466457	20040210
US 7098229	B2	20060829		

PRIORITY APPLN. INFO.:

WO 2002-US845	W	20020111
US 2004-466457	A1	20040210
US 2006-442743	A2	20060530
US 2001-758883	A	20010111

AB The present invention provides novel compns. and methods for the controlling appetite and weight and/or treating obesity using a (+)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane or related compound The invention also provides novel compns. and methods for treating or preventing disorders related to or complicated by excessive body weight or obesity, including coronary heart disease, osteoarthritis, osteoporosis, dyslipidemias, gout, atherosclerosis, joint pain, sexual and fertility problems, respiratory problems, gall bladder disease, skin conditions, hypertension, diabetes, stroke, pulmonary embolism, sleep apnea, idiopathic intracranial hypertension, lower extremity venous stasis disease, gastro-esophageal reflux, urinary stress incontinence, metabolic syndrome, insulin resistance and cancer. The methods and compns. of the invention may employ a (+)-1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane or related compound alone, or in combination with a second anti-appetite or anti-obesity agent.

IT 2295-31-0D, Thiazolidinedione, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for controlling body weight and appetite)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:969931 CAPLUS

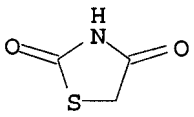
10/ 507,399

DOCUMENT NUMBER: 147:314998
TITLE: Single nucleotide polymorphisms in the human PPARα gene associated with weight gain in PPAR agonist therapy of diabetes
INVENTOR(S): Ranade, Koustubh
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: U.S. Pat. Appl. Publ., 198pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2007202512	A1	20070830	US 2006-505577		20060817
PRIORITY APPLN. INFO.:			US 2005-709733P	P	20050819
			US 2005-710018P	P	20050819

AB Single nucleotide polymorphisms (SNPs) in the human peroxisome proliferator-activated receptor α (PPARα) gene that are associated with weight gain in the treatment of type 2 diabetes with thiazolidinediones are identified. These SNPs can be used to select diabetes therapies that may include knockdown of genes carrying SNPs with adverse effects. They can also be used to lower levels of glycosylated HbA1C. Primers and probes for detection of these polymorphisms are also described.

IT 2295-31-0D, Thiazolidinedione, derivs.
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (as antidiabetics; SNPs human PPARα gene associated with weight gain in PPAR agonist therapy of diabetes)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:789111 CAPLUS
DOCUMENT NUMBER: 147:173633
TITLE: Combination of triazine derivatives and insulin sensitizers
INVENTOR(S): Moinet, Gerard; Cravo, Daniel; Mesangeau, Didier
PATENT ASSIGNEE(S): Merck Patent GmbH, Germany
SOURCE: PCT Int. Appl., 34pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007079917	A2	20070719	WO 2006-EP12185	20061218
WO 2007079917	A3	20070830		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,

MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

FR 2896159	A1	20070720	FR 2006-344	20060113
PRIORITY APPLN. INFO.:			FR 2006-344	A 20060113

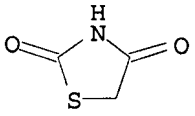
OTHER SOURCE(S): MARPAT 147:173633

AB The present invention relates to combinations of triazine derivs. and of insulin sensitizers. Thus, a formulation contained muraglitazar 5, and (+)-2-amino-3,6-dihydro-4-dimethylamino-6-methyl-1,3,5-triazine-HCl 1000 mg in addition to conventional excipients.

IT 2295-31-0D, 2,4-Thiazolidinedione, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of triazine derivs. and insulin sensitizers)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:761334 CAPLUS
DOCUMENT NUMBER: 147:166196
TITLE: Bicyclic nitrogen compounds as modulators of ghrelin receptor and their preparation, pharmaceutical compositions and use in the treatment of diseases
INVENTOR(S): Burstein, Ethan; Eeg Knapp, Anne; Olsson, Roger; Eskildsen, Jorgen; Ek, Fredrik
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 481pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007079239	A2	20070712	WO 2006-US49609	20061229

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2007213359	A1	20070913	US 2006-618724	20061229
PRIORITY APPLN. INFO.:			US 2005-755714P	P 20051230

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US 2006-835241P P 20060802

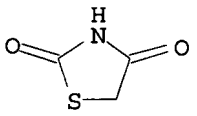
OTHER SOURCE(S): MARPAT 147:166196
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed herein are compds. of formula I as defined herein, or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof, that modulates the activity of a ghrelin receptor. Disclosed herein are also methods of treating diseases or conditions that comprise administering to a subject in need thereof a therapeutically effective amount of a compound of formula I. Compds. of formula I wherein A is H, halo, CN, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted (hetero)aryl, etc.; B is H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted (hetero)aryl, etc.; Y is CR3 and N R2 and R2a are independently H, CN, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted (hetero)aryl, etc; R3, R3a, R3b, and R3c are independently H, halo, CN, NO2, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted (hetero)aryl, etc.; L is (un)substituted alkylene; L can be taken together with R3 to form a cycloalkyl, cycloalkenyl, cycloalkynyl and heteroalicyclyl; and their solvates, polymorphs, metabolites, pharmaceutically acceptable salts and prodrugs thereof, are claimed. Example compound II was prepared by amination of 1-[1-(3-chlorophenoxy)-7-methoxy-1H-indol-3-yl]ethanone with 4-(4-fluorophenoxy)piperidine hydrochloride; the resulting compound II was added oxalic acid to give the corresponding salt. All the invention compds. were evaluated for their ghrelin receptor modulatory activity (some data given).

IT 2295-31-0, Thiazolidinedione
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of bicyclic nitrogen compds. as modulators of ghrelin receptors for treating various diseases)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:633849 CAPLUS
DOCUMENT NUMBER: 147:225897
TITLE: Review article: drug hepatotoxicity
AUTHOR(S): Chang, C. Y.; Schiano, T. D.
CORPORATE SOURCE: The Division of Liver Diseases, Department of Internal Medicine, The Mount Sinai School of Medicine, New York, NY, USA
SOURCE: Alimentary Pharmacology and Therapeutics (2007), 25(10), 1135-1151
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

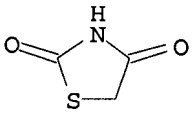
AB A review. Background: Drug toxicity is the leading cause of acute liver

failure in the United States. Further understanding of hepatotoxicity is becoming increasingly important as more drugs come to market. Aims: (i) To provide an update on recent advances in our understanding of hepatotoxicity of select commonly used drug classes. (ii) To assess the safety of these medications in patients with pre-existing liver disease and in the post-liver transplant setting. (iii) To review relevant advances in toxicogenomics which contribute to the current understanding of hepatotoxic drugs. Methods: A Medline search was performed to identify relevant literature using search terms including 'drug toxicity, hepatotoxicity, statins, thiazolidinediones, antibiotics, antiretroviral drugs and toxicogenomics'. Results: Amoxicillin-clavulanic acid is one of the most frequently implicated causes of drug-induced liver injury worldwide. Statins rarely cause clin. significant liver injury, even in patients with underlying liver disease. Newer thiazolidinediones are not associated with the degree of liver toxicity observed with troglitazone. Careful monitoring for liver toxicity is warranted in patients who are taking antiretrovirals, especially patients who are co-infected with hepatitis B and C. Genetic polymorphisms among enzymes involved in drug metabolism and HLA types may account for some of the differences in individual susceptibility to drug hepatotoxicity. Conclusions Drug-induced hepatotoxicity will remain a problem that carries both clin. and regulatory significance as long as new drugs continue to enter the market. Future results from ongoing multicentre collaborative efforts may help contribute to our current understanding of hepatotoxicity associated with drugs.

IT 2295-31-0, Thiazolidinedione
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(newer thiazolidinediones were not associated with degree of liver toxicity observed with troglitazone in patient with liver disease and liver transplantation)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 152 THERE ARE 152 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:526910 CAPLUS

DOCUMENT NUMBER: 147:158088

TITLE: Response to pioglitazone treatment is associated with the lipoprotein lipase S447X variant in subjects with type 2 diabetes mellitus

AUTHOR(S): Wang, G.; Wang, X.; Zhang, Q.; Ma, Z.

CORPORATE SOURCE: Department of Endocrinology, Peking University Third Hospital, Beijing, Peop. Rep. China

SOURCE: International Journal of Clinical Practice (2007), 61(4), 552-557
CODEN: IJCPF9; ISSN: 1368-5031

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

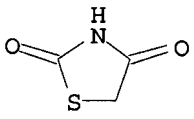
LANGUAGE: English

AB To investigate the influence of the S447X variant in lipoprotein lipase (LPL) gene on the response rate to therapy with the thiazolidinedione

pioglitazone. A total of 113 diabetic patients were treated with pioglitazone 30 mg for 10 wk. Response to the pioglitazone treatment was defined by either a >10% relative reduction in fasting blood glucose (FBG) or a more than 1% decrease in glycosylated Hb (HbA1c) values after 10 wk of pioglitazone treatment. The genotypes were determined by polymerase chain reaction-restriction fragment length polymorphism method. Using the criteria >10% relative reduction in FBG after 10 wk of pioglitazone treatment, responder frequency to pioglitazone treatment in S447S genotype group is significantly higher than S447X genotype group. Meanwhile, the S447X genotype conferred a statistically significant 0.538-fold reduction in response rate to pioglitazone treatment relative to the S447S genotype. Moreover, pioglitazone treatment has significantly beneficial effects on serum lipid profile and blood pressure in S447S genotype carriers. The S447X variant in LPL gene may be a cause for therapy modification by pioglitazone.

IT 2295-31-0, Thiazolidinedione
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipoprotein lipase S447X variant was associated with high response of pioglitazone treatment in type 2 diabetes mellitus patient)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:384921 CAPLUS
DOCUMENT NUMBER: 146:395304
TITLE: Genetic markers associated with responses to insulin sensitizers and their use in selecting therapies for disorders of glucose metabolism
INVENTOR(S): McCamish, Mark A.
PATENT ASSIGNEE(S): Perlegen Sciences, Inc., USA
SOURCE: PCT Int. Appl., 122pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007038670	A2	20070405	WO 2006-US37821	20060929
WO 2007038670	A3	20070920		

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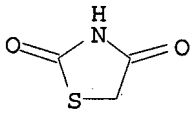
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.: US 2005-722357P P 20050930
US 2005-722636P P 20050930

AB Single nucleotide polymorphisms associated with adverse responses to insulin-sensitizing drugs are identified for use in the selection of these drugs in the treatment of disorders of glucose metabolism The insulin sensitizer for which the individual is screened and the insulin sensitizer that is administered or not administered may be the same or different. In another aspect, the invention provides methods comprising identifying one or more genetic variations, e.g., one or more single nucleotide polymorphisms, that at least partly differentiate between a subset of a plurality of individuals who experience a response when administered an insulin sensitizer, and a subset of said plurality of individuals who do not experience a response when administered the insulin sensitizer. The invention also provides nucleic acids, polypeptides, antibodies, kits, and business methods associated with these screening and association methods.

IT 2295-31-0D, Thiazolidinedione, derivs.
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as insulin sensitizers, selection of; genetic markers associated with responses to insulin sensitizers and their use in selecting therapies for disorders of glucose metabolism)

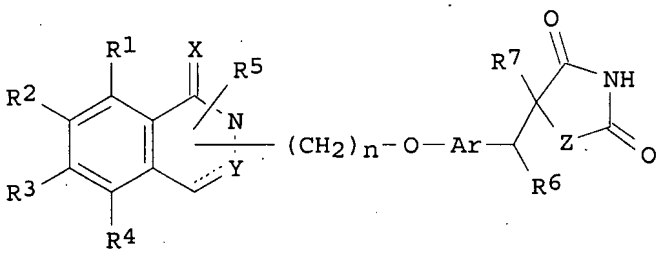
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:181159 CAPLUS
DOCUMENT NUMBER: 147:322999
TITLE: Preparation of heterocyclic compounds as antidiabetic, hypolipidemic, and antihypertensive agents
INVENTOR(S): Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Rao, Paraselli Bheema; Madhavan, Gurram Ranga; Rajagopalan, Ramanujam; Chakrabarti, Ranjan
PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, India
SOURCE: Indian Pat. Appl., 44pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 1998MA01147	A	20050304	IN 1998-MA1147	19980528

PRIORITY APPLN. INFO.: IN 1998-MA1147 19980528
GI



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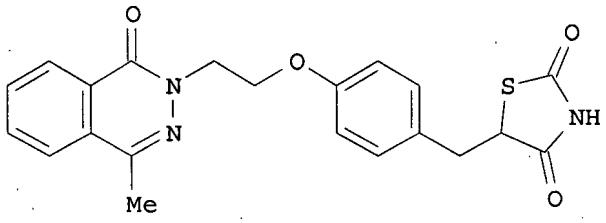


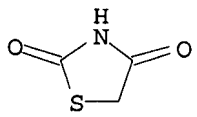
II

AB The title heterocyclic compds. I [wherein X = O or S; Y = O or N; Z = O or S; R1-R4 = independently H, halo, OH, CN, NO2, etc.; when connected to carbon atom, R5 = H, OH, halo, NO2, etc.; or when connected to nitrogen atom, R5 = H, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, etc.; Ar = (un)substituted divalent phenylene, naphthylene, pyridyl, quinolinyl, etc.; R6 and R7 = independently H, OH, halo, or alkyl; or R6 and R7 together form a bond; n = 1-4; with provisos], or tautomers, stereoisomers, polymorphs, pharmaceutically acceptable salts, or solvates thereof were prepared for treatment of diabetes, hyperlipidemia, and hypertension. For example, II was prepared in a multi-step synthesis. In vivov test, II reduced 61% blood glucose. Formulations were also described.

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as antidiabetic, hypolipidemic, and antihypertensive agents)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:143943 CAPLUS

DOCUMENT NUMBER: 146:222536

TITLE: Methods of assessing risk for premature coronary artery disease and myocardial infarction by detecting single nucleotide polymorphisms in PPARγ and resistin genes and diagnostic and therapeutic applications

INVENTOR(S): Burnett, Mary Susan; Devaney, Joseph M.; Epstein, Stephen E.

PATENT ASSIGNEE(S): Medstar Research Institute, Inc., USA

SOURCE: PCT Int. Appl., 35pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

10/ 507,399

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007016558	A2	20070208	WO 2006-US29920	20060731
WO 2007016558	A3	20070531		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

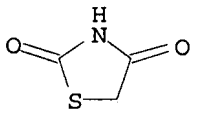
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-704145P P 20050729
US 2005-704167P P 20050729

AB The present invention provides methods of assessing risk for premature coronary artery disease (CAD) and myocardial infarction by detecting single nucleotide polymorphisms (SNPs) in PPARγ and resistin genes. An association between the Ala allele of the P12A variant of the human PPARγ gene and development of CAD, particularly premature CAD, in Caucasian women is described. Methods for decreasing CAD risk in patients with P12A polymorphism are provided by administering thiazolidinediones or other PPARγ agonists. SNPs in the human resistin gene associated with CAD include T167C, G233A, C980G and G1325A. The C980G polymorphism is associated with premature CAD in men.

IT 2295-31-0, Thiazolidinedione
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PPARγ as target for; methods of assessing risk for premature coronary artery disease and myocardial infarction by detecting SNPs in PPARγ and resistin genes and diagnostic and therapeutic applications)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1285854 CAPLUS
DOCUMENT NUMBER: 146:45500
TITLE: Substituted biarylheterocycle derivatives as protein kinase inhibitors and their preparation, pharmacokinetics, pharmaceutical compositions and their use in the treatment of cancer and other diseases
INVENTOR(S): Young, Yang; Young, Pranee; Miranda, Martin; Pfahl, Michaela; Carter, Bruce; Muthalif, Mubarack; Pfahl, Magnus
PATENT ASSIGNEE(S): The Pfahl Family Trust, USA
SOURCE: PCT Int. Appl., 68pp.
CODEN: PIXXD2

10/ 507,399

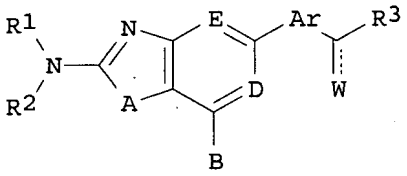
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006130613	A2	20061207	WO 2006-US20986	20060530
WO 2006130613	A3	20070208		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-686062P P 20050531
OTHER SOURCE(S): MARPAT 146:45500
GI



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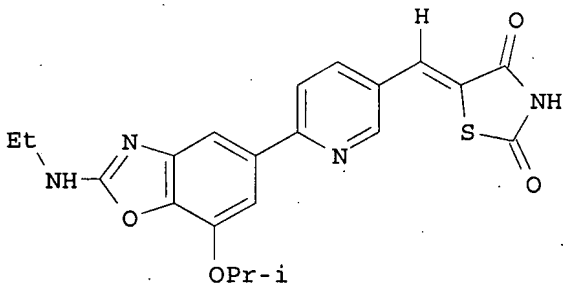


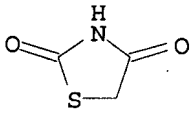
II

AB The invention is directed to certain patentable substituted benzoxazole derivs. of formula I that exhibit protein kinase (PK) inhibition activity or modulating ability. Compds. of formula I wherein dotted line is absent or present; W is 2,4-dioxothiazolidin-5-yl(idene); acetal; A is (un)substituted methylene, NH and derivs., O, and S; B is OH an derivs., SH and derivs., and NH2 and derivs.; D and E together or independently (un)substituted CH and N; Ar is pyridinyl and phenylene; and their isomers, metabolites, polymorphs, prodrugs and salts thereof are claimed. Pharmaceutical compns. comprising these compds., and methods for preparing and using them, are also described. For example, these heterocyclic compds. are useful in treating disorders related to abnormal PK activity, including diseases and disorders involving aberrant cell proliferation, for example, AML, CML, gastrointestinal stromal cancers,

thyroid cancer, other cancers and leukemias, as well as other diseases such as inflammation and atherosclerosis. Example compound II was prepared by bromination of 2-isopropoxyphenol; the resulting 4-bromo-2-isopropoxyphenol underwent silylation with tert-butyldimethylsilyl chloride to give (4-bromo-2-isopropoxyphenoxy)tert-butyldimethylsilane which underwent boration to give the corresponding phenylboronic acid, which underwent cross-coupling with 4-bromopyridine-3-carboxyaldehyde to give 6-[4-(tert-butyldimethylsilanyloxy)-3-isopropoxyphenyl]pyridine-3-carboxaldehyde which underwent desilylation to give the corresponding phenol, which under went nitration to give the corresponding nitrophenol, which underwent acetalization and reduction to give 2-amino-4-(5-[1,3]dioxolan-2-ylpyridin-2-yl)-6-isopropoxyphenol, which underwent cyclization with cyanogen bromide to give 5-(5-diethoxymethylpyridin-2-yl)-7-isopropoxybenzooxazol-2-ylamine, which underwent hydrolysis to give the corresponding aldehyde, which underwent N-alkylation and condensation with thiazolidine-2,4-dione to give compound II. All the invention compds. were evaluated for their protein kinase inhibitory activity (data give).

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted benzoxazole derivs. with protein kinase modulating ability useful in treatment of diseases)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1253003 CAPLUS
DOCUMENT NUMBER: 146:804
TITLE: insulin sensitization for delaying puberty and increasing growth
INVENTOR(S): De Zegher, Francis; Dunger, David; Ibanez, Lourdes
PATENT ASSIGNEE(S): K.U. Leuven Research and Development, Belg.; Addenbrooke's Hospital
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

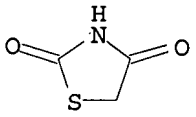
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006125285	A1	20061130	WO 2006-BE60	20060523
WO 2006125285	B1	20070111		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

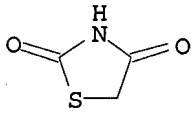
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

10/ 507,399

PRIORITY APPLN. INFO.: GB 2005-10469 A 20050523
OTHER SOURCE(S): MARPAT 146:804
AB In accordance with the purpose of the invention, as embodied and broadly described herein, the invention is broadly drawn to a new method of treatment, the use of agents to manufacture a composition of treatment or the composition of treatment for the prevention of rapidly progressive puberty, the prevention of early menarche or the modulation, more particularly the delay, of the tempo of puberty in a female mammal, preferably a human girl, and the disorders related thereto. In a particular embodiment the present invention involves the use of at least one insulin-sensitizing agent such as metformin, any of the polymorphs of metformin or a pharmaceutically acceptable salt thereof for the preparation of a composition of treatment to modulate the tempo of pubertal progression in a girl. Metformin administration to girls experiencing precocious puberty resulted in normalization of pubertal progression to menarche, increased height gains, leaner body composition, and decreases indexes relating to insulin resistance.
IT 2295-31-0, Glitazone 2295-31-0D, Glitazone, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metformin-induced insulin sensitization for delaying puberty and increasing growth)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1150755 CAPLUS
DOCUMENT NUMBER: 145:455005
TITLE: Preparation of diphenyl ethers and analogs for lowering the plasm level of glucose, fatty acids, cholesterol and triglycerides
INVENTOR(S): Neogi, Partha; Nag, Bishwajit; Dey, Debendranath; Nag, Abhijeet; Bhattacharya, Birendra Kumar; Singh, Vinod Kumar; Jayakumar, Surendradoss
PATENT ASSIGNEE(S): Bexel Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 19pp., Cont.-in-part of U.S. Ser. No. 96,718.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

10/ 507,399

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006247285	A1	20061102	US 2006-359657	20060221
US 2004142991	A1	20040722	US 2003-356113	20030131
US 6794401	B2	20040921		
US 2005096366	A1	20050505	US 2004-947047	20040921
US 2005288341	A1	20051229	US 2005-96718	20050331
WO 2007097992	A2	20070830	WO 2007-US4007	20070215

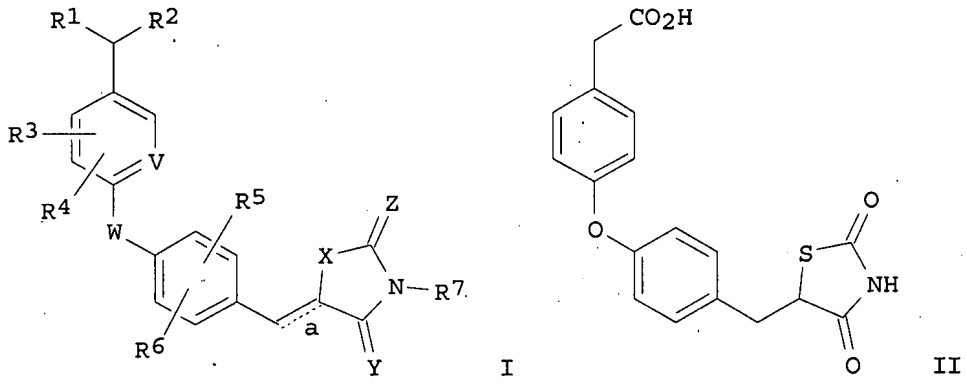
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

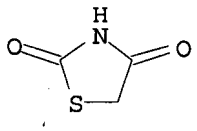
US 2003-356113	A1	20030131
US 2004-947047	B2	20040921
IN 2005-DE347	A	20050214
US 2005-96718	A2	20050331
US 2003-440772P	P	20030117
US 2006-359657	A	20060221

GI



AB Title compds. I [a = single or double bond; V = CH or N; Y = O or S; W = O, NH or N(alkyl); X = CR9, O or S; R9 is H or R9 and Z may link together to form a ring; Z = O or S; R1 - R6 = H, halo, OH, etc.; R7 = H, (un)substituted alkyl, alkenyl, aryl, etc.;] and their analogs, tautomeric forms, stereoisomers, polymorphs, hydrates, or pharmaceutically acceptable salts and solvates, which are effective in lowering the plasm level of glucose, fatty acids, cholesterol and triglycerides, and are useful in the treatment and/or prophylaxis of such as diabetes, were prepared. For instance, etherification of 4-hydroxyphenylacetic acid with 4-fluorobenzaldehyde (25.6%) followed by condensation with 2,4-thiazolidinedione (85.4%) and subsequent hydrogenation of the resultant alkene with Pd/C-ammonium formate gave II. This product and its disodium salt were found to induce glucose uptake over basal levels at a

concentration of 1.0 μM, while they did not show any toxicity at a concentration of
100 μM. Other biol. activities were also tested.
IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of di-Ph ethers and analogs for lowering the plasm level of glucose, fatty acids, cholesterol and triglycerides)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:733033 CAPLUS
DOCUMENT NUMBER: 145:174316
TITLE: Direct compression formulation comprising dipeptidylpeptidase IV inhibitor
INVENTOR(S): Pfeffer, Sabine; Schaefer, Frank; Schneeberger, Ricardo; Sutton, Paul Allen; Trueby, Martin Friedrich; Wirth, Wolfgang
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006078593	A2	20060727	WO 2006-US1473	20060117
WO 2006078593	A3	20060914		
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006206670	A1	20060727	AU 2006-206670	20060117
CA 2593359	A1	20060727	CA 2006-2593359	20060117
US 2006210627	A1	20060921	US 2006-333582	20060117
EP 1841413	A2	20071010	EP 2006-718534	20060117
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
IN 2007DN04530	A	20070831	IN 2007-DN4530	20070613

PRIORITY APPLN. INFO.:

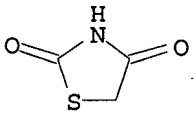
US 2005-644645P	P	20050118
US 2005-690484P	P	20050614
WO 2006-US1473	W	20060117

AB This invention relates to tablets especially tablets formed by direct compression of a dipeptidylpeptidase IV (DPP-IV) inhibitor compound, a process for the preparation thereof, to new pharmaceutical formulations, and

new tableting powders comprising DPP-IV inhibitor formulations capable of being directly compressed into tablets. The invention relates further to a process for preparing the tablets by blending the active ingredient and specific excipients into the new formulations and then directly compressing the formulations into the direct compression tablets. The invention also relates to vildagliptin particle size distribution and a new crystal form of vildagliptin particularly adapted for the preparation of improved tablets and other pharmaceutical compns. For example, tablets were produced containing LAF237 100 mg , microcryst. cellulose 191,36 mg, lactose anhydrous 95.64 mg, sodium starch glycolate 8 mg and magnesium stearate 5 mg.

IT 2295-31-0, Glitazone
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(direct compression formulation comprising dipeptidylpeptidase IV inhibitor)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)

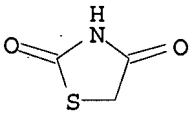


L4 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:689663 CAPLUS
DOCUMENT NUMBER: 145:142210
TITLE: Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome
AUTHOR(S): Kadowaki, Takashi; Yamauchi, Toshimasa; Kubota, Naoto; Hara, Kazuo; Ueki, Kohjiro; Tobe, Kazuyuki
CORPORATE SOURCE: Department of Metabolic Diseases, Graduate School of Medicine, University of Tokyo, Tokyo, Japan
SOURCE: Journal of Clinical Investigation (2006), 116(7), 1784-1792
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Adiponectin is an adipokine that is specifically and abundantly expressed in adipose tissue and directly sensitizes the body to insulin. Hypoadiponectinemia, caused by interactions of genetic factors such as SNPs in the Adiponectin gene and environmental factors causing obesity, appears to play an important causal role in insulin resistance, type 2 diabetes, and the metabolic syndrome, which are linked to obesity. The adiponectin receptors, AdipoR1 and AdipoR2, which mediate the antidiabetic metabolic actions of adiponectin, have been cloned and are downregulated in obesity-linked insulin resistance. Upregulation of adiponectin is a partial cause of the insulin-sensitizing and antidiabetic actions of thiazolidinediones. Therefore, adiponectin and adiponectin receptors represent potential versatile therapeutic targets to combat obesity-linked diseases characterized by insulin resistance. This Review describes the pathophysiol. of adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome.

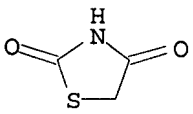
IT 2295-31-0, 2,4-Thiazolidinedione
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TZD (thiazolidinedione); Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



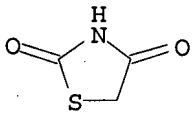
REFERENCE COUNT: 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:616604 CAPLUS
DOCUMENT NUMBER: 145:452850
TITLE: The 11482G>A polymorphism in the perilipin gene is associated with weight gain with rosiglitazone treatment in type 2 diabetes
AUTHOR(S): Kang, Eun Seok; Cha, Bong Soo; Kim, Hyeong Jin; Kim, Hae Jin; Kim, So Hun; Hur, Kyu Yeon; Lee, Hyun Joo; Shim, Wan Sub; Ahn, Chul Woo; Lee, Hyun Chul
CORPORATE SOURCE: Department of Internal Medicine, Yonsei University College of Medicine, Seoul, S. Korea
SOURCE: Diabetes Care (2006), 29(6), 1320-1324
CODEN: DICAD2; ISSN: 0149-5992
PUBLISHER: American Diabetes Association, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB OBJECTIVE: The aim of this study was to examine the effects of perilipin gene (PLIN) polymorphisms on weight gain with rosiglitazone treatment in patients with type 2 diabetes. RESEARCH DESIGN AND METHODS: A total of 160 type 2 diabetic patients were treated with rosiglitazone (4 mg/day) for 12 wk in addition to their previous medications, which were unchanged. Four single nucleotide polymorphisms (SNPs) at the PLIN locus were genotyped: PLIN 6209T>C, PLIN 11482G>A, PLIN 13041A>G, and PLIN 14995A>T. RESULTS: Although fasting plasma glucose and HbA1c levels decreased; mean body weight increased significantly after rosiglitazone treatment. Among the four SNPs tested, only the PLIN 11482G>A polymorphism was associated with weight gain from rosiglitazone treatment. In addition, there was a significant difference in the increase in the body weight among the genotypes. Patients with the 11482A/A genotype showed less increase in body weight than those with other genotypes. CONCLUSIONS: These data suggest that genetic variations in the perilipin gene can affect weight gain associated with rosiglitazone treatment in patients with type 2 diabetes.
IT 2295-31-0, Thiazolidinedione
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(perilipin gene 11482G >A polymorphism was associated with weight gain with thiazolidinedione rosiglitazone treatment in type 2 diabetic patient)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:217610 CAPLUS
DOCUMENT NUMBER: 145:179920
TITLE: Effect of genetic polymorphisms in cytochrome P450 (CYP) 2C9 and CYP2C8 on the pharmacokinetics of oral antidiabetic drugs: clinical relevance
AUTHOR(S): Kirchheiner, Julia; Roots, Ivar; Goldammer, Mark; Rosenkranz, Bernd; Brockmoeller, Juergen
CORPORATE SOURCE: Institute of Clinical Pharmacology, University Medical Center Charite, Humboldt University, Berlin, Germany
SOURCE: Clinical Pharmacokinetics (2005), 44(12), 1209-1225
CODEN: CPKNDH; ISSN: 0312-5963
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Type 2 diabetes mellitus affects up to 8% of the adult population in Western countries. Treatment of this disease with oral antidiabetic drugs is characterized by considerable interindividual variability in pharmacokinetics, clin. efficacy and adverse effects. Genetic factors are known to contribute to individual differences in bioavailability, drug transport, metabolism and drug action. Only scarce data exist on the clin. implications of this genetic variability on adverse drug effects or clin. outcomes in patients taking oral antidiabetics. The polymorphic enzyme cytochrome P 450 (CYP) 2C9 is the main enzyme catalyzing the biotransformation of sulfonylureas. Total oral clearance of all studied sulfonylureas (tolbutamide, glibenclamide [glyburide], glimepiride, glipizide) was only about 20% in persons with the CYP2C9*3/*3 genotype compared with carriers of the wild-type genotype CYP2C9*1/*1, and clearance in the heterozygous carriers was between 50% and 80% of that of the wild-type genotypes. For reasons not completely known, the resulting differences in drug effects were much less pronounced. Nevertheless, CYP2C9 genotype-based dose adjustments may reduce the incidence of adverse effects. The magnitude of how doses might be adjusted can be derived from pharmacokinetic studies. The meglitinide-class drug nateglinide is metabolized by CYP2C9. According to the pharmacokinetic data, moderate dose adjustments based on CYP2C9 genotypes may help in reducing interindividual variability in the antihyperglycemic effects of nateglinide. Repaglinide is metabolized by CYP2C8 and, according to clin. studies, CYP2C8*3 carriers had higher clearance than carriers of the wild-type genotypes; however, this was not consistent with in vitro data and therefore further studies are needed. CYP2C8*3 is closely linked with CYP2C9*2. CYP2C8 and CYP3A4 are the main enzymes catalyzing biotransformation of the thiazolidinediones troglitazone and pioglitazone, whereas rosiglitazone is metabolized by CYP2C9 and CYP2C8. The biguanide metformin is not significantly metabolized but polymorphisms in the organic cation transporter (OCT) 1 and OCT2 may determine its pharmacokinetic variability. In conclusion, pharmacogenetic variability plays an important role in the pharmacokinetics of oral antidiabetic drugs; however, to date, the impact of this variability on clin. outcomes in patients is mostly unknown and prospective studies on the medical benefit of CYP genotyping are required.
IT 2295-31-0, Thiazolidinedione
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytochrome P 450 2C8 and cytochrome P 450 3A4 enzymes catalyzed biotransformation of thiazolidinediones troglitazone and pioglitazone in human)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

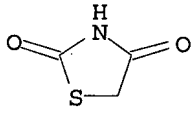
L4 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:300702 CAPLUS
DOCUMENT NUMBER: 142:367684
TITLE: Polymorphisms in phosphatidylinositol 3-kinase catalytic subunit p110β gene aassoicated with development of insulin resistance in obese children and methods for therapy
INVENTOR(S): Bougneres, Pierre
PATENT ASSIGNEE(S): Pfizer Health AB, Swed.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005031341	A2	20050407	WO 2004-IB3926	20040928
WO 2005031341	A3	20050728		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005118622	A1	20050602	US 2004-951579	20040928
PRIORITY APPLN. INFO.:			US 2003-507226P P	20030929
			US 2004-587333P P	20040713

AB The present invention relates to polymorphisms in phosphatidylinositol 3-kinase catalytic subunit p110β gene associated with development of insulin resistance in obese children and methods for therapy. Methods for treating or preventing insulin resistance using thiazolidinedione compds. are provided.

IT 2295-31-0, Thiazolidinedione
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphisms in phosphatidylinositol 3-kinase catalytic subunit p110β gene aassoicated with development of insulin resistance in obese children and methods for therapy)

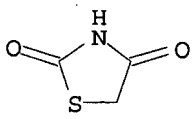
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:216663 CAPLUS
DOCUMENT NUMBER: 142:266828
TITLE: Preparation of pharmaceutical compositions of nateglinide
INVENTOR(S): Singh, Romi Barat; Shilpa, Anu; Nagaprasad, Vishnubhotla; Sethi, Sanjeev Kumar
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020979	A1	20050310	WO 2004-IB51678	20040902
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003DE01100	A	20050527	IN 2003-DE1100	20030903
IN 2006DN01688	A	20070810	IN 2006-DN1688	20060328
PRIORITY APPLN. INFO.:			IN 2003-DE1100 A	20030903
			WO 2004-IB51678 W	20040902

AB The present invention relates to a pharmaceutical composition comprising nateglinide, and a process for its preparation Thus, a formulation contained nateglinide 120, lactose monohydrate 325, colloidal silicon dioxide 40.8, microcryst. cellulose 86, polyvinylpyrrolidone 12, croscarmellose sodium 32.8, sodium lauryl sulfate 12, magnesium stearate 11.4 mg/tablet and water q.s.
IT 2295-31-0D, 2,4-Thiazolidinedione, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pharmaceutical compns. of nateglinide)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:197009 CAPLUS
DOCUMENT NUMBER: 143:303896
TITLE: Association of peroxisome proliferator-activated receptor gamma 2 Pro-12-Ala-polymorphism with endometriosis

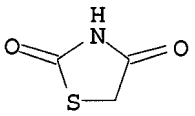
10/ 507,399

AUTHOR(S): Dogan, Songuel; Machicao, Fausto; Wallwiener, Diethelm; Haering, Hans-Ulrich; Diedrich, Klaus; Hornung, Daniela
CORPORATE SOURCE: Department of Gynecology and Obstetrics and Dep of Endocrinology and Metabolism, University of Tuebingen, Tuebingen, Germany
SOURCE: Fertility and Sterility (2004), 81(5), 1411-1413
CODEN: FESTAS; ISSN: 0015-0282
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The association of peroxisome proliferator-activated receptor gamma 2, (PPAR)-α, Pro-12-Ala polymorphism with endometriosis was investigated in a case-control study with 51 Caucasian women with endometriosis stages I-IV and 55 Caucasian control women without endometriosis. Results show a high frequency of the Pro-12-Ala polymorphism in patients with endometriosis compared with in women without endometriosis. The frequency was even higher in cases with at least one recurrence of endometriosis, suggesting that the 12-Pro allele may have protective effects against implantation and growth of ectopic endometrial fragments, while the 12-Ala allele might facilitate the development, progression, and recurrence of endometriosis.

IT 2295-31-0, Thiazolidinedione
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(association of peroxisome proliferator-activated receptor gamma 2 Pro-12-Ala-polymorphism with endometriosis)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:23834 CAPLUS
DOCUMENT NUMBER: 143:279485
TITLE: Advances of nuclear transcription factor: peroxisome proliferator-activated receptor γ2
AUTHOR(S): Sun, Yuru; Yang, Ze
CORPORATE SOURCE: National Institute of Geriatrics, Beijing Hospital ,Ministry of Health, Beijing, 100730, Peop. Rep. China
SOURCE: Yichuan (2003), 25(6), 713-717
CODEN: ICHUDW; ISSN: 0253-9772
PUBLISHER: Yichuan Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

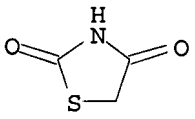
AB A review with 32 refs. on advances of nuclear translation factor peroxisome proliferator-activated receptor γ2 including the structure of PPARγ2 and its expression, the regulation of PPARγ2, the polymorphism of PPARγ2 and the mechanism of the association of PPARγ2 with disease. The role in adipocyte differentiation, the common Pro12→Alα polymorphism associated with obesity and type 2 diabetes, and the function as the target mol. of thiazolidinediones diabetes drug are reviewed.

IT 2295-31-0, Thiazolidinedione
RL: PAC (Pharmacological activity); BIOL (Biological study)

10/ 507,399

(PPARγ2 transcription inhibition by; advances of nuclear transcription factor peroxisome proliferator-activated receptor γ2)

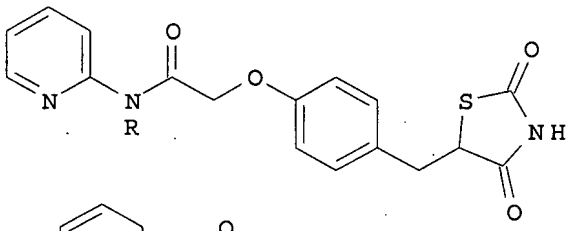
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



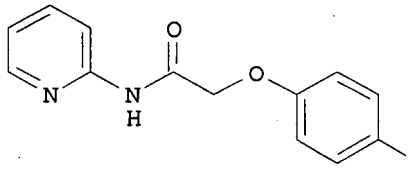
L4 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:878396 CAPLUS
DOCUMENT NUMBER: 141:350162
TITLE: Rosiglitazone derivatives and putative metabolites as antidiabetic agents and process for their preparation
INVENTOR(S): Kumar, Yatendra; Gowrishankar, Radhakrishnan; Aryan, Ram Chander; Bhushan, Kumar Hari; Mishra, Manoj Kumar
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089945	A1	20041021	WO 2004-IB1108	20040408
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: IN 2003-DE590 A 20030409
OTHER SOURCE(S): CASREACT 141:350162; MARPAT 141:350162
GI



I



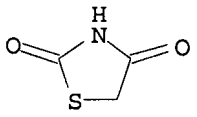
II

AB The invention relates to rosiglitazone derivs. I (R = H or C1-C4 alkyl), their pharmaceutically acceptable salts, solvates, hydrates or polymorphs, process for their preparation, pharmaceutical compns. comprising them, and methods of using them for the treatment and/or prophylaxis of hyperglycemia, hyperlipidemia and hypertension. Compds. I are putative metabolites of rosiglitazone. It is hypothesized (no data) that conversion of the N-adjacent CH2 group in rosiglitazone to CO, as in I, would improve the pharmacol. profile and possibly increase potency. For example, alkylation of 4-hydroxybenzaldehyde with bromoacetic acid in the presence of K2CO3 followed by coupling with 2-aminopyridine using DCC as coupling reagent gave aldehyde II. Treatment of II with 2,4-thiazolidinedione in the presence of pyrrolidine and subsequent reduction of the resultant alkene with NaBH4 yielded I (R = H). I (R = Me) was also prepared in a similar manner.

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; rosiglitazone derivs. as antidiabetic agents and process for their preparation)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:589256 CAPLUS

DOCUMENT NUMBER: 141:140764

TITLE: Preparation of amino acid phenoxy ethers as inhibitors of cytokines

INVENTOR(S): Nag, Bishwajit; Nag, Abhijeet; Dey, Debendranath; Agarwal, Shiv Kumar

PATENT ASSIGNEE(S): Bexel Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 47 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

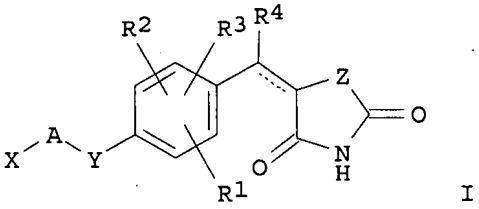
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004142991	A1	20040722	US 2003-356113	20030131
US 6794401	B2	20040921		
AU 2004207449	A1	20040812	AU 2004-207449	20040113
CA 2513496	A1	20040812	CA 2004-2513496	20040113
WO 2004066964	A2	20040812	WO 2004-US790	20040113
WO 2004066964	A9	20040902		
WO 2004066964	A3	20050224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1583529	A2	20051012	EP 2004-701752	20040113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2004006772	A	20051227	BR 2004-6772		20040113
CN 1758907	A	20060412	CN 2004-80006737		20040113
JP 2007501288	T	20070125	JP 2006-536536		20040113
US 2005096366	A1	20050505	US 2004-947047		20040921
US 2005288341	A1	20051229	US 2005-96718		20050331
MX 2005PA07684	A	20060310	MX 2005-PA7684		20050718
IN 2005KN01481	A	20060714	IN 2005-KN1481		20050728
NO 2005003714	A	20051011	NO 2005-3714		20050801
US 2006247285	A1	20061102	US 2006-359657		20060221
PRIORITY APPLN. INFO.:			US 2003-440772P	P	20030117
			US 2003-356113	A	20030131
			WO 2004-US790	W	20040113
			US 2004-947047	A2	20040921
			IN 2005-DE347	A	20050214
			US 2005-96718	A2	20050331

OTHER SOURCE(S): MARPAT 141:140764

GI



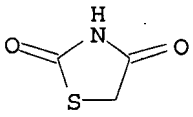
I

AB Novel amino acid Ph ethers, e.g. tyrosine Ph ethers, or tautomeric forms, stereoisomers, polymorphs, pharmaceutically acceptable salts, or pharmaceutically acceptable solvates thereof [I; wherein the dotted line represents an optional double bond; Y = O, S, NR (wherein R represents hydrogen or alkyl); Z = O, S; R1-R4 = H, halogen, HO, nitro, cyano, formyl, amino, alkyl, alkoxy; A = a bond or substituted or unsubstituted aryl, heterocyclyl or heteroaryl ring; X = an alpha aminocarboxylic acid or alpha aminocarboxylic acid derivative bonded to A or Y through its alpha side chain] are prepared Also provided are a method for reducing glucose, free fatty acids, cholesterol, or triglyceride levels in plasma,. These compds. inhibit cytokines such as TNFα, IL-6, and IL-1β and exhibit activity for the treatment of immunol. diseases mediated by cytokines, autoimmune diseases such as multiple sclerosis and rheumatoid arthritis, inflammation mediated by cyclooxygenase, obesity, hyperlipidemia, hypertension, neurol. diseases and diabetes, or a disorder associated with insulin resistance. Unlike other thiazolidine-compds. (TZD mols.), the compds. I exhibit no adipocyte differentiation, reduce body weight gain, and appear to have no affinity for PPAR-g and thereby are different from known TZD mols., which typically have adipocyte differentiation activity, increase weight gain, and are PPAR-g agonists. Thus, Me 2-[(tert-butoxycarbonyl)amino]-3-(4-hydroxyphenyl)propanoate was treated with NaH in DMF and etherified with 4-Fluorobenzaldehyde at 80° to give Me 2-[(tert-butoxycarbonyl)amino]-3-[-(4-formylphenoxy)phenyl]propanoate which was condensed with 2,4-thiazolidinedione in the presence of benzoic acid and piperidine at 145-155° under reflux with continuous removal of water using Dean-Stark apparatus for 5 h followed by treatment with HCl in CH2Cl2 to give 5-[4-[4-(2-amino-2-methoxycarbonylethyl)phenoxy]benzylidene]thiazolidine-2,4-dione hydrochloride (II). Catalytic hydrogenation of II over Pd/C in methanol gave 5-[4-[4-(2-amino-2-methoxycarbonylethyl)phenoxy]benzyl]thiazolidine-2,4-dione (III). III lowered pro-inflammatory cytokines in human

macrophage cells and in an animal model of inflammation inhibited carrageenan-induced paw edema in SD rats.

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of tyrosine thiazolidinylmethylphenyl ether derivs. for treatment of immunol. diseases, inflammation, obesity, hyperlipidemia, hypertension, neurol. diseases, and diabetes)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

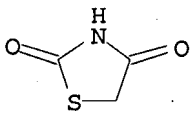
L4 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:554357 CAPLUS
DOCUMENT NUMBER: 141:188642
TITLE: Plasma cell membrane glycoprotein 1 (PC-1): a marker of insulin resistance in obesity, uremia and diabetes mellitus
AUTHOR(S): Stefanovic, Vladisav; Antic, Slobodan
CORPORATE SOURCE: Faculty of Medicine, Institute of Nephrology and Hemodialysis, Nis, Yugoslavia
SOURCE: Clinical Laboratory (Heidelberg, Germany) (2004), 50(5+6), 271-278
CODEN: CLLAFP; ISSN: 1433-6510
PUBLISHER: Verlag Klinisches Labor
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Insulin resistance is a characteristic feature of obesity and type 2 diabetes mellitus, but it is also present in up to 25% of healthy nonobese individuals. The mol. mechanisms causing insulin resistance are not yet fully understood. Recently, overexpression of several potential inhibitors of the insulin receptor tyrosine-kinase activity, a key step in insulin signaling, has been described in insulin-resistant subjects. PC-1 is expressed in many tissues and inhibits insulin signaling either at the level of the insulin receptor or downstream at a postreceptor site. An elevated PC-1 content in insulin target tissues may play an important role in the development of insulin resistance in obesity and type 2 diabetes mellitus. A polymorphism in PC-1 has been demonstrated to be associated with insulin resistance. This was a DNA polymorphism in exon 4 that causes an amino acid change from lysine to glutamine at codon 121 (K121Q). PC-1 121Q allele might predispose independently of other well established risk factors for early myocardial infarction. Testing for the PC-1 K121Q polymorphism might be valuable in patients with a family history of atherosclerotic vascular disease and myocardial infarction. There is growing evidence that genetic factors play an important role in the development of diabetic nephropathy (DN). Efforts to identify these factors rely primarily on the candidate gene approach; candidate genes for insulin resistance may be considered candidates for DN as well. In a stratified anal. according to duration of diabetes, the risk of early-onset end-stage renal disease (ESRD) for carriers of the Q variant was 2.3 times that for noncarriers. The cellular mechanisms for the insulin resistance of pregnancy and gestational diabetes mellitus (GDM) are unknown. Women with GDM have an increased PC-1 content and excessive phosphorylation of serine/threonine residues in muscle insulin receptors. The postreceptor defects in insulin signaling may contribute

to the pathogenesis of GDM and the increased risk for type 2 diabetes later in life. Although widely explored, the true cause of insulin resistance in uremic patients is not entirely elucidated yet. During the last decade it was found that erythropoietin (EPO) therapy, used for correction of anemia in patients with end stage renal failure, ameliorates insulin resistance. An increased lymphocyte PC-1 activity over control was found in hemodialysis patients. A two-month EPO therapy significantly decreased PC-1 activity to the control values, suggesting that an effect on PC-1 expression could be implicated in the amelioration of insulin resistance in uremic patients treated with EPO. Current investigations implicate that therapeutic modification of PC-1 expression would be of great benefit for insulin-resistant type 2 diabetics. Metformin, a biguanide oral antidiabetic agent, was shown to affect insulin resistance by decreasing enzymic activity of overexpressed PC-1 mols. in obese type 2 diabetics. Thiazolidinedione (TZD) insulin-sensitizing drugs are a class of compds. that improve insulin action in vivo. Treatment of patients with TZDs seems to have a beneficial effect on most, if not all, components of metabolic syndrome. TZDs have also been used in the treatment of nondiabetic human insulin-resistant states, and have demonstrated an improvement in insulin sensitivity. Although much remains to be learned about PPAR γ receptor and TZD action, the advent of TZD insulin-sensitizing agents has an enormous impact on the understanding of insulin resistance. The great potential of insulin resistance therapy illuminated by the TZDs will continue to catalyze research in this area directed toward the discovery of new insulin-sensitizing agents that work through other mechanisms.

IT 2295-31-0, Thiazolidinedione
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasma cell membrane glycoprotein PC-1 as marker of insulin resistance in obesity, uremia and diabetes)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:633683 CAPLUS
DOCUMENT NUMBER: 139:185673
TITLE: Preparation and compositions of polymorphic forms of bicyclic antidiabetic agents
INVENTOR(S): Srisilla, Raju; Potlapally, Rajender Kumar; Mamillapalli, Ramabhadra Sarma; Gaddam, Om Reddy
PATENT ASSIGNEE(S): Reddy's Laboratories Limited, India
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003066612	A1	20030814	WO 2003-IB408	20030207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

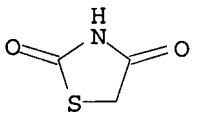
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 2002MA00095	A	20050304	IN 2002-MA95		20020207
AU 2003244514	A1	20030902	AU 2003-244514		20030207
PRIORITY APPLN. INFO.:			IN 2002-MA95	A	20020207
			WO 2003-IB408	W	20030207

AB This invention relates to novel polymorphic/pseudopolymorphic forms and compns. of arginine salt of 3-[4-[2-(3,4-dihydro-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxypropanoic acid, preferably, L-arginine salt of (2S)-3-[4-[2-(3,4-dihydro-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxypropanoic acid. The polymorphic forms of the present invention are more active, as antidiabetic and hypolipidemic agent, than the 3-[4-[2-(2,3-dihydro-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxypropanoic acid.

IT 2295-31-0D, Thiazolidinedione, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; preparation and compns. of polymorphic forms of arginine salt of benzothiazine antidiabetic/hypolipidemic agent)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:551189 CAPLUS
DOCUMENT NUMBER:	139:101121
TITLE:	Preparation of 1,1'-biphenyl derivatives as biaromatic ligand activators of peroxisome proliferator-activated receptors subtype gamma (PPAR gamma receptors)
INVENTOR(S):	Bernardon, Jean-Michel; Clary, Laurence; Terranova, Eric
PATENT ASSIGNEE(S):	Galderma Research & Development S.N.C., Fr.
SOURCE:	U.S. Pat. Appl. Publ., 23 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003134885	A1	20030717	US 2002-326054	20021223
US 6908939	B2	20050621		
FR 2833949	A1	20030627	FR 2001-16750	20011221
FR 2833949	B1	20050805		
FR 2836683	A1	20030905	FR 2002-2647	20020301
FR 2836683	B1	20060623		
US 2005137238	A1	20050623	US 2005-42212	20050126

US 7122564	B2	20061017			
US 2007043046	A1	20070222	US 2006-505879		20060818
PRIORITY APPLN. INFO.:			FR 2001-16750	A	20011221
			US 2002-351425P	P	20020128
			FR 2002-2647	A	20020301
			US 2002-326054	A3	20021223
			US 2005-42212	A3	20050126

OTHER SOURCE(S): MARPAT 139:101121

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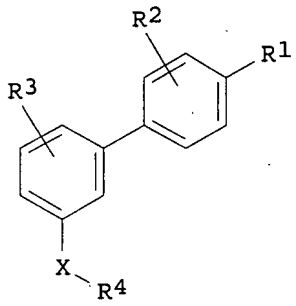
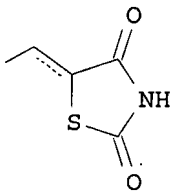
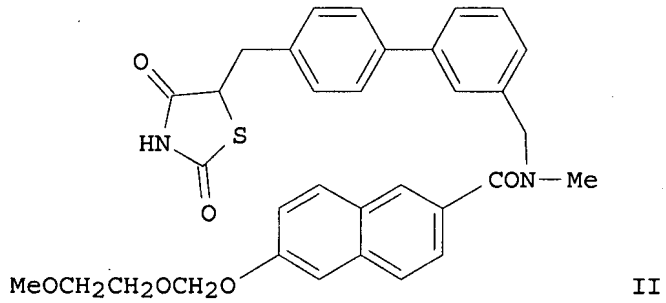


I

Q=





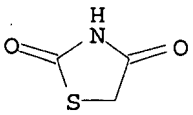
II

AB The title compds. [I; R1 = Q, CH2CHR6COR5; R2, R3 = H, C1-6 alkyl, aryl, halo, HO, C1-6 alkoxy, aryloxy, aralkyloxy, a polyether radical, NO2, C1-6 alkyl-(un)substituted NH2 group; X = N-(un)substituted CH2NHCO, NHCONH, NHCOCH2, or NHCH2CO whether read from left to right or vise versa; R4 = each (un)substituted Ph, benzyl, phenethyl, thienyl, furyl, or pyridyl; R5 = HO, C1-9 alkoxy; R6 = C1-6 alkyl, OR14, SR14; wherein R14 = C1-12 alkyl, CF3, aryl, aralkyl] are prepared Novel pharmaceutical/cosmetic compns. contain at least one biarom. ligand activator of a PPARγ receptor, such biarom. ligand having the structural formula I and are well suited, inter alia, for regulating and/or restoring skin lipid metabolism, for treating a wide variety of dermatol. afflictions, and for preventing and/or treating the signs of aging and/or dry skin. Thus, 1.27 g 5-(3'-methylaminomethylbiphenyl-4-ylmethyl)thiazolidine-2,4-dione was condensed with 1.97 g 6-(2-methoxyethoxymethoxy)naphthalene-2-carboxylic acid using 1-hydroxybenzotriazole, Et3N, and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in CH2Cl2 at room temperature for 3 h to give 1.97 g (62%) of 6-(2-methoxyethoxymethoxy)-N-[4'-(2,4-dioxothiazolidin-5-ylmethyl)biphenyl-3-ylmethyl]-N-methylnaphthalene-2-carboxamide (II). II in vitro activated PPARα and PPARγ receptors expressed in Hela cells by 22.9 and 93.3%, resp., with AC50 of >50,000.0 and 0.55 nM, resp. (AC50 = 50% activation of the basal signal relative to the reference agonist (-)-3-[4-[2-(benzoxazol-2-

ylmethylamino)ethoxy]phenyl]-2-ethoxypropionic acid). Various formulations containing specific I compds., e.g. tablet containing II, were illustrated.

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of biphenyl derivs. as biarom. ligand activators of peroxisome proliferator-activated receptors subtype γ for treating skin diseases and preventing and/or treating the signs of aging and/or dry skin)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

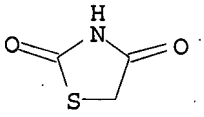
L4 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:474774 CAPLUS
DOCUMENT NUMBER: 139:223509
TITLE: The metabolic syndrome: Peroxisome proliferator-activated receptor γ and its therapeutic modulation
AUTHOR(S): Gurnell, Mark; Savage, David B.; Chatterjee, V. Krishna K.; O'Rahilly, Stephen
CORPORATE SOURCE: Department of Medicine, Addenbrooke's Hospital, University of Cambridge, Cambridge, CB2 2QQ, UK
SOURCE: Journal of Clinical Endocrinology and Metabolism (2003), 88(6), 2412-2421
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. By the end of this decade, it has been estimated that between 200 million and 300 million people worldwide will meet World Health Organization diagnostic criteria for diabetes mellitus. This epidemic of predominantly type 2 diabetes has largely been mediated by our shift toward a more sedentary lifestyle predisposing to obesity and insulin resistance. Affected individuals can also exhibit an array of associated undesirable traits such as hypertension, dyslipidemia, and hypercoagulability, leading to morbidity and mortality from atherosclerotic vascular disease. The coexistence of several of these traits with insulin resistance constitutes the metabolic syndrome. Accordingly, improving insulin sensitivity in this group, and thereby potentially ameliorating the excess vascular risk, is a primary goal of treatment. Recent interest has focused on the thiazolidinediones, a novel class of antidiabetic agents, which act as insulin sensitizers and, therefore, potentially target the underlying metabolic disturbance. These agents are high-affinity ligands for the nuclear receptor peroxisome proliferator-activated receptor γ, and a large body of in vitro and in vivo data has evolved to support their increasing clin. use. Importantly, clin. and laboratory findings in human subjects harboring natural mutations and polymorphisms within the receptor have provided addnl. insights. Here, we focus on the consequences of inherited variation in the human peroxisome proliferator-activated receptor γ gene, linking this receptor to disordered glucose homeostasis, adipogenesis, lipid metabolism, and blood pressure regulation. These studies provide further support for the future development of more selective

receptor modulators, targeting specific pathways to ameliorate facets of the metabolic syndrome.

IT 2295-31-0, Thiazolidinedione
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PPAR-γ and its therapeutic modulation of metabolic syndrome)

RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

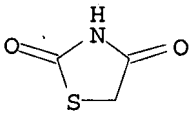
L4 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:259781 CAPLUS
DOCUMENT NUMBER: 138:282435
TITLE: Methods for detecting polymorphic A-C repeat Z-allele sequence of aldose reductase gene associated with benefiting from diabetes mellitus therapeutic agents
INVENTOR(S): Fryburg, David Albert; Klioze, Solomon Samuel; Milos, Patrice Marie; Oates, Peter Joseph
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1298223	A2	20030402	EP 2002-256379	20020916
EP 1298223	A3	20030723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2404723	A1	20030328	CA 2002-2404723	20020923
BR 2002003865	A	20030916	BR 2002-3865	20020924
JP 2003180399	A	20030702	JP 2002-278779	20020925
MX 2002PA09566	A	20030312	MX 2002-PA9566	20020927
US 2003114357	A1	20030619	US 2002-256877	20020927
PRIORITY APPLN. INFO.:			US 2001-325927P P	20010928

AB This invention relates to methods of characterizing subjects and methods of treatment or prevention of diseases and pathol. conditions relating to the polymorphic A-C repeat sequence located approx. 2.1 kb upstream from the aldose reductase gene. Polymorphic A-C repeat Z-allele sequence of aldose reductase gene are associated with benefiting from diabetes mellitus therapeutic agents.

IT 2295-31-0, Thiazolidinedione
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for detecting polymorphic A-C repeat Z-allele sequence of aldose reductase gene associated with benefiting from diabetes mellitus therapeutic agents)

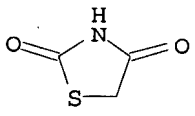
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:784737 CAPLUS
DOCUMENT NUMBER: 136:95447
TITLE: Insulin resistance and insulin sensitizers
AUTHOR(S): Stumvoll, Michael; Haering, Hans
CORPORATE SOURCE: Medizinische Klinik, Abteilung fur Endokrinologie, Stoffwechsel und Pathobiochemie, Eberhard-Karls-Universitaet, Tuebingen, Germany
SOURCE: Hormone Research (2001), 55(Suppl. 2), 3-13
CODEN: HRMRA3; ISSN: 0301-0163
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Insulin resistance is a key factor in the pathogenesis of type 2 diabetes mellitus and a co-factor in the development of dyslipidemia, hypertension and atherosclerosis. The causes of insulin resistance include factors such as obesity and phys. inactivity, and there may also be genetic factors. The mechanism of obesity-related insulin resistance involves the release of factors from adipocytes which exert a neg. effect on glucose metabolism: free fatty acids, tumor necrosis factor-α and the recently discovered hormone, resistin. The two resulting abnormalities observed consistently in glucose-intolerant states are impaired suppression of endogenous glucose production, and impaired stimulation of glucose uptake. Among the genetic factors, a polymorphism (Pro12Ala) in the peroxisome proliferator-activated receptor (PPAR) γ is associated with a reduced risk of type 2 diabetes mellitus and increased insulin sensitivity, primarily that of lipolysis. On the other hand, the association with insulin resistance of a common polymorphism (Gly972Arg) in the insulin receptor substrate 1, long believed to be a plausible candidate gene, is weak at best. This polymorphism may instead be associated with reduced insulin secretion, which, in view of the recent recognition of the insulin signalling system in β-cells, results in the development of a novel pathogenic concept. Finally, fine-mapping and positional cloning of the susceptibility locus on chromosome 2 resulted in the identification of a polymorphism (UCSNP-43 G/A) in the calpain-10 gene. In non-diabetic Pima Indians, this polymorphism was associated with insulin resistance of glucose disposal. The pharmacol. treatment of insulin resistance has recently acquired a novel class of agents: the thiazolidinediones. They act through regulation of PPARγ-dependent genes and probably interfere favorably with factors released from adipocytes which mediate obesity-associated insulin resistance.

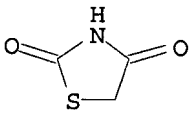
IT 2295-31-0D, Thiazolidinedione, compds.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin resistance and insulin sensitizers)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR

THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

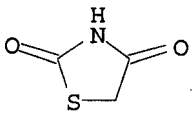
L4 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:522672 CAPLUS
DOCUMENT NUMBER: 135:235813
TITLE: PPARγ/RXR as a molecular target for diabetes
AUTHOR(S): Lenhard, James M.
CORPORATE SOURCE: Department of Metabolic Diseases, GlaxoSmithKline Inc., Research Triangle Park, NC, 27709, USA
SOURCE: Receptors and Channels (2001), 7(4), 249-258
CODEN: RCHAE4; ISSN: 1060-6823
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 141 refs. Type 2 diabetes is associated with insulin resistance in peripheral tissues, such as muscle and fat. Novel therapies that improve insulin action include ligands that bind and activate the nuclear receptors peroxisome proliferator activating receptor γ (PPARγ) and retinoid X receptor (RXR). PPARγ/RXR form heterodimers that regulate transcription of genes involved in insulin action, adipocyte differentiation, lipid metabolism and inflammation. PPARγ activators include prostanoids, fatty acids, thiazolidinediones and N-(2-benzoylphenyl)tyrosine analogs. RXR ligands include naturally occurring retinoic acid and synthetic rexinoids. Selective ligands for these receptors improve metabolic abnormalities associated with type 2 diabetes, such as hyperglycemia, hyperlipidemia, insulin resistance and other cardiovascular risk factors. Although adipose tissue mediates some of the effects of PPARγ/RXR ligands, other tissues also regulate the effects of these receptors. The activity of the PPARγ/RXR heterodimer is influenced by posttranslational modifications, receptor turnover, polymorphisms, splice variants, coactivators and corepressors. This article reviews recent developments in research on these receptors, with particular emphasis on metabolic effects, ligand selectivity, structure and regulation of the PPARγ/RXR heterodimer.
IT 2295-31-0D, Thiazolidinedione, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PPARγ/RXR as therapeutic target for diabetes)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 141 THERE ARE 141 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:752997 CAPLUS
DOCUMENT NUMBER: 134:291030
TITLE: Transcriptional activation of the human ucp1 gene in a rodent cell line. Synergism of retinoids, isoproterenol, and thiazolidinedione is mediated by a multipartite response element
AUTHOR(S): Del Mar Gonzalez-Barroso, Maria; Pecqueur, Claire;

Gelly, Chantal; Sanchis, Daniel; Alves-Guerra, Marie-Clotilde; Bouillaud, Frederic; Ricquier, Daniel; Cassard-Doulcier, Anne-Marie
CORPORATE SOURCE: Centre de Recherches sur l'Endocrinologie Moleculaire et le Developpement, CNRS, Meudon, 92190, Fr.
SOURCE: Journal of Biological Chemistry (2000), 275(41), 31722-31732
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Uncoupling protein 1 (UCP1) is uniquely expressed in brown adipocytes and generates heat production by uncoupling respiration from ATP synthesis. The activatory effects of norepinephrine and retinoic acid (RA) on rodent ucp1 gene transcription have been well characterized. These effects are mediated by a 211-base pair (bp) enhancer which is also sufficient to restrict expression to brown adipose tissue. The mol. mechanisms controlling the transcription of the human ucp1 gene are unknown. In order to study the transcriptional regulation of the human gene, we set up chloramphenicol acetyltransferase constructs containing the entire or deleted 5' regions upstream of the transcriptional start site of the gene. These constructs were transiently transfected in a mouse cell line. A 350-bp hormone response region showing a significant homol. with the rat ucp1 enhancer and located between the BclI polymorphic site and an AatII site (bp -3820/-3470) was detected. This region was sufficient to mediate the stimulation by RA and by combined treatments (RA + isoproterenol (ISO), RA + thiazolidinedione (TZD), or RA + ISO + TZD). The highest stimulation, a 26-fold increase in basal activity, was obtained by RA + ISO + TZD treatment. In contrast to the rodent gene, under our conditions, the effect of ISO and/or TZD is dependent on RA stimulation. Anal. of 105 bp inside the 350-bp element by site-directed mutagenesis and gel retardation expts. demonstrated that a multipartite response element mediates the drug stimulation. This region binds RARs and RXRs nuclear factors, CREB/ATF factors, and also PPARγ despite the absence of a consensus peroxisome-proliferator response element. The activation of the human ucp1 gene transcription by certain hormones or drugs, and the identification of the cis-elements involved, will help to identify new compds. activating fat oxidation and energy expenditure in humans.
IT 2295-31-0, Thiazolidinedione
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(stimulation of ucp1 gene promoter by; transcriptional activation of the human ucp1 gene in a rodent cell line. Synergism of retinoids, isoproterenol, and thiazolidinedione is mediated by a multipartite response element)
RN 2295-31-0 CAPLUS
CN 2,4-Thiazolidinedione (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:212642 CAPLUS
DOCUMENT NUMBER: 130:223293

10/ 507,399

TITLE: Heterocyclic compounds, process for their preparation and pharmaceutical compositions containing them and their use in the treatment of diabetes and related diseases

INVENTOR(S): Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Paraselli, Rao Bheema

PATENT ASSIGNEE(S): Reddy's Research Foundation, India; Reddy-Cheminor, Inc.

SOURCE: U.S., 26 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5885997	A	19990323	US 1996-777627	19961231
IN 1996MA01150	A	20050304	IN 1996-MA1150	19960701
CA 2258949	A1	19971106	CA 1997-2258949	19970630
WO 9741097	A2	19971106	WO 1997-US11522	19970630
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9737198	A	19971119	AU 1997-37198	19970630
AU 744518	B2	20020228		
US 5985884	A	19991116	US 1997-884816	19970630
EP 958296	A1	19991124	EP 1997-934041	19970630
EP 958296	B1	20030730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
BR 9711098	A	20000308	BR 1997-11098	19970630
CN 1275982	A	20001206	CN 1997-195778	19970630
JP 2002515874	T	20020528	JP 1997-539307	19970630
IL 127296	A	20030112	IL 1997-127296	19970630
RU 2200161	C2	20030310	RU 1998-123195	19970630
AT 246190	T	20030815	AT 1997-934041	19970630
PT 958296	T	20031128	PT 1997-934041	19970630
HU 2003001101	A2	20031229	HU 2003-1101	19970630
ES 2199366	T3	20040216	ES 1997-934041	19970630
IL 142649	A	20041215	IL 1997-142649	19970630
PL 192664	B1	20061130	PL 1997-342608	19970630
ZA 9705866	A	19980223	ZA 1997-5866	19970701
MX 9810782	A	20001130	MX 1998-10782	19981215
NO 9806055	A	19981222	NO 1998-6055	19981222
NO 313699	B1	20021118		
US 6114526	A	20000905	US 1999-353286	19990714
US 6310069	B1	20011030	US 2000-535387	20000324
US 6573268	B1	20030603	US 2000-535388	20000324
HK 1026204	A1	20050121	HK 2000-103109	20000524
US 2001031759	A1	20011018	US 2001-827009	20010405
US 6372750	B2	20020416		
US 2002123502	A1	20020905	US 2001-32846	20011226
US 6780992	B2	20040824		
US 39266	E1	20060905	US 2003-697926	20031030
US 2005032864	A1	20050210	US 2004-917221	20040812

PRIORITY APPLN. INFO.:		
IN 1996-MA1150	A	19960701
US 1996-777627	A	19961231
IL 1997-127296	A3	19970630

US 1997-884816	A	19970630
WO 1997-US11522	W	19970630
US 1999-353286	A3	19990714
US 2000-535387	E	20000324
US 2000-535388	A3	20000324
US 2001-827009	A3	20010405
US 2001-32846	A1	20011226

OTHER SOURCE(S): MARPAT 130:223293

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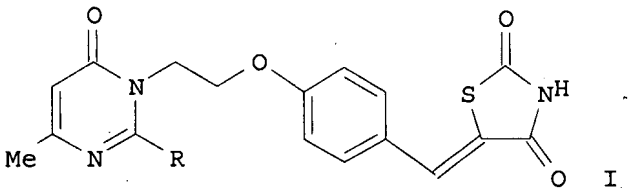
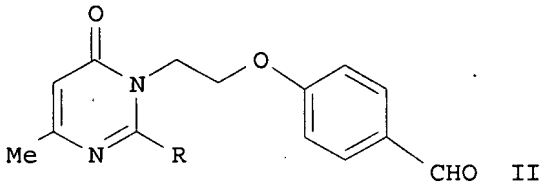


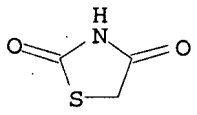


AB The present invention relates to novel antidiabetic compds., their tautomeric forms, their derivs., their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compns. containing them. This invention particularly relates to novel azolidinedione derivs., and their pharmaceutically acceptable salts, pharmaceutically acceptable solvates and pharmaceutical compns. containing them. Approx. 30 title compds. such as I (R = Pr, Me, Et, Bu, benzyl) and their quinazoline analogs were prepared in 66-99% yields, e.g., by condensation of aldehydes II with thiazolidine-2,4-dione. Antidiabetic data was given for several of the prepared compds. At 30 mg/kg/day, after 6 days, 5-[4-[2-[2-ethyl-4-methyl-6-oxo-1,5-dihydro-1-pyrimidinyl]ethoxy]phenylmethyl] thiazolidine-2,4-dione reduced the blood glucose level 73%, lowered triglycerides 70% and also lowered cholesterol in the rat.

IT 2295-31-0, Thiazolidine-2,4-dione
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimidinylethoxybenzylthiazolidinediones)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)

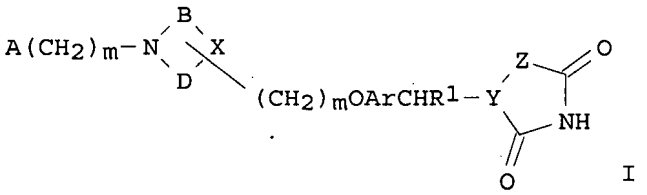


REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:740228 CAPLUS
DOCUMENT NUMBER: 128:13264
TITLE: Novel heterocyclic compounds having antidiabetic, hypolipidemic, antihypertensive properties, process for their preparation and pharmaceutical composites
INVENTOR(S): Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Bajji, Ashok Channaveerappa; Alla, Sekar Reddy; Ramanujam, Rajagopalan; Chakrabarti, Ranjan
PATENT ASSIGNEE(S): Reddy-Cheminor, Inc., India; Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Bajji, Ashok Channaveerappa; Alla, Sekar Reddy; Ramanujam, Rajagopalan; Chakrabarti, Ranjan; Dr. Reddy's Research Foundation
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9741121	A1	19971106	WO 1997-US7416	19970502
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9728237	A	19971119	AU 1997-28237	19970502
EP 894089	A1	19990203	EP 1997-922610	19970502
EP 894089	B1	20021023		
R: CH, DE, FR, GB, LI, SE				
CN 1221416	A	19990630	CN 1997-195251	19970502
JP 2001518068	T	20011009	JP 1997-539252	19970502
US 5889025	A	19990330	US 1997-851450	19970505

PRIORITY APPLN. INFO.: WO 1997-US7416 W 19970502
OTHER SOURCE(S): CASREACT 128:13264; MARPAT 128:13264
GI



I

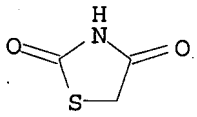
AB The present invention relates to novel antidiabetic compds., their tautomeric forms, their derivs., their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compns. containing them. This invention particularly relates to novel azolidinedione derivs. I (A represents substituted or fused, single or fused, aromatic group or substituted or unsubstituted, single or fused, heterocyclic group with 1 or more hetero atoms of O, N or S; B and D represent substituted or unsubstituted linking group between N and X which

maybe satd, or may contain 1 or more double bonds; X represents either a CH2 group or a hetero atom of N, O or S; Ar represents an optionally substituted divalent single or fused aromatic or heterocyclic group; R1 = H, OH, alkoxy, halo, or lower alkyl group or forms a bond together with the adjacent group Y; Y = N or a group CR2 where R2 = H, OH, alkoxy, halo or lower alkyl or R2 forms a bond together with R1; Z = O or S when Y = CR2 and Z = O when Y = N; m = 1-4; n = 0-4) and their pharmaceutically acceptable salts, pharmaceutically acceptable solvates and pharmaceutical compns. containing them.

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of thiazolidinediones as antidiabetic, hypolipidemic and antihypertensive agents)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:740227 CAPLUS

DOCUMENT NUMBER: 128:13260

TITLE: Thiazolidinedione compounds having antidiabetic, hypolipidemic, antihypertensive properties, process for their preparation and pharmaceutical compositions

INVENTOR(S): Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Alla, Sekar Reddy; Paraselli, Rao Bheema; Ramanujam, Rajagopalan; Chakrabarti, Ranjan

PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, India; Reddy-Cheminor, Inc.; Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Alla, Sekar Reddy; Paraselli, Rao Bheema; Ramanujam, Rajagopalan; Chakrabarti, Ranjan

SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9741120	A1	19971106	WO 1997-US7415	19970502
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5801173	A	19980901	US 1996-687840	19960726
AU 9729954	A	19971119	AU 1997-29954	19970502
EP 923580	A1	19990623	EP 1997-924560	19970502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1221417	A	19990630	CN 1997-195279	19970502
JP 2000514041	T	20001024	JP 1997-539251	19970502

PRIORITY APPLN. INFO.: US 1996-687840 A1 19960726

WO 1997-US7415 W 19970502

OTHER SOURCE(S): CASREACT 128:13260; MARPAT 128:13260

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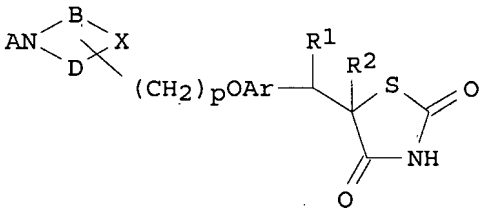


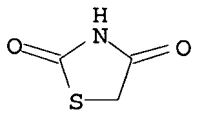
I

AB Novel thiazolidinedione antidiabetic compds. I [A = (un)substituted aromatic or 5-membered O-, N-, or S-containing heterocyclic group which may be fused to (un)substituted 6-membered N-containing heterocyclic group, which also may be fused; B, D = (un)substituted hydrocarbon linking group; X = CH2, N, O, S; Ar = (un)substituted divalent aromatic or heterocyclic group; R1, R2 = H, lower alkyl, halo, alkoxy, OH, or R1R2 = bond; p = 0-4] were prepared along with their tautomeric forms, their derivs., their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceuticals and acceptable compns. containing them. Methods for preparing the antidiabetic compds. and their uses are claimed.

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of thiazolidinediones having antidiabetic, hypolipidemic and antihypertensive properties)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)



L4 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:740226 CAPLUS

DOCUMENT NUMBER: 128:13259

TITLE: Novel antidiabetic compounds having hypolipidemic, antihypertensive properties, process for their preparation and pharmaceutical compositions containing them

INVENTOR(S): Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Alla, Sekar Reddy; Ramanujam, Rajagopalan; Chakrabarti, Ranjan

PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, India; Reddy-Cheminor, Inc.; Lohray, Vidya Bhushan; Lohray, Braj Bhushan; Alla, Sekar Reddy; Ramanujam, Rajagopalan; Chakrabarti, Ranjan

SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

10/ 507,399

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9741119	A1	19971106	WO 1997-US7417	19970502
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9729307	A	19971119	AU 1997-29307	19970502
EP 981526	A1	20000301	EP 1997-923526	19970502
EP 981526	B1	20040225		
R: CH, DE, FR, GB, LI, SE				
JP 2001518069	T	20011009	JP 1997-539253	19970502
PRIORITY APPLN. INFO.:			WO 1997-US7417 W	19970502
OTHER SOURCE(S):	CASREACT 128:13259; MARPAT 128:13259			

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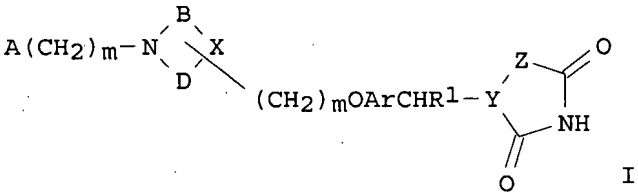


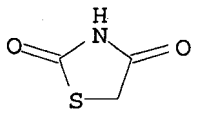
I

AB New thiazolidine-2,4-dione derivs. I (A = substituted or unsubstituted, single or fused, aromatic group or substituted or unsubstituted, single or fused, heterocyclic group with 1 or more hetero atoms selected from N, O, S; W = O, S, NR2 where R2 = H or lower alkyl group; Q = heteroatom of O, S or NR3 group where R3 = H or lower alkyl or lower alkoxy group; B and D = substituted or unsubstituted hydrocarbon linking group between N and X which may be saturated or may contain 1 or more double bonds; X = CH2 or hetero atom of N, S or O; Ar = optionally substituted divalent single or fused aromatic or optionally substituted single or fused heterocyclic group; R1 = H, OH, alkoxy, halo or lower alkyl group or forms a bond together with adjacent group Y; Y = = N or CR6 group where R6 = H, OH, alkoxy, halo or lower alkyl group or R2 forms a bond together with R1; Z = O or S when Y = CR2 ad Z = O when Y = N; m = 1-4; n = 0-4) their tautomeric forms, their derivs., their stereoisomers, their polymorphs, their pharmaceutical acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compns. containing them are claimed. Methods for their preparation and their use as antidiabetic compds. are claimed.

IT 2295-31-0, 2,4-Thiazolidinedione
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of thiazolidine-2,4-dione derivs. as antidiabetic and antihypertensives and hypolipemic agents)

RN 2295-31-0 CAPLUS

CN 2,4-Thiazolidinedione (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 17:25:03 ON 22 OCT 2007)

FILE 'REGISTRY' ENTERED AT 17:25:17 ON 22 OCT 2007
L1 0 S GLITAZONE AND POTASSIUM
L2 2 S GLITAZONE

FILE 'CAPLUS' ENTERED AT 17:26:28 ON 22 OCT 2007
L3 2013 S L2
L4 34 S L3 AND POLYMORPH?

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	182.13	198.09
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-26.52	-26.52

STN INTERNATIONAL LOGOFF AT 17:27:44 ON 22 OCT 2007